# 1. 'A' Allele, CYP2D6'3, A21337 deletion, Frameshift resulting in zero enzyme activity 2637

### Appln. No. 09/880,732 Amendment dated October 25, 2004 Response to Drawing Requirement of August 25, 2004

	Replace Replace	eement Sheet	, 2004
CYPwt (+) A2624, 22mer,54%GC, Tm=63-64C CYPwt (+) A2624 (A) 30-3'NH2 CYPwt (+) A2625 (A) 30-3'NH2 CYPwt (+) A2625b (A) 30-3'NH2 CYPwut (+) A2624,21 mer,57%GC, Tm=61-63C CYPmut (+) A2624 (A) 30-3'NH2 CYPmut (+) A2625 (A) 30-3'NH2 CYPmut (+) A2625 (A) 30-3'NH2	<pre>Wild Type(+) Mut(+) s activity +)B1922 (A/C to mut at base 13) CYDwr(-)R1922 17mer 76%GC Tm=66C</pre>	\ \alpha	B1930,1 B1930(A),1 B1930(A),1 B1930,
5'- GCTAACTGAGCACGGATGACC -3' NH2 5'- GCTAACTGAGCACAGGATGACC (A) 30 -3' NH2 5'- CTAACTGAGCACAGGATGACC (A) 30 -3' NH2 5'- CTAACTGAGCACAGGATGAC (A) 30 -3' NH2 5'- GCTAACTGAGCAC-GGATGACC -3'NH2 5'- GCTAACTGAGCAC-GGATGACC (A) 30 -3' NH2 5'- CTAACTGAGCAC-GGATGACC (A) 30 -3' NH2 5'- CTAACTGAGCAC-GGATGACC (A) 30 -3' NH2 5'- CTAACTGAGCAC-GGATGACC (A) 30 -3' NH2	-2612 ID NO:14 5'- GCTGGATGAGCTGCACAGGATGACCTGGGACCCAGCC -3' Wild Type(+) ID NO:15 5'- GCTGGATGAGCTGCTAACTGAGCAC-GGATGACCTGGGACCCAGCCCAG		NH2 3' - GGGTCCTGCGGGGAI  NH2 3' - GGGTCCTGCGGGGAI  S' - CCCAAGACGCCCCTT  5' - CCCAAGACGCCCCTT  - CCCTTACCCGCATCTCCCACGACGCCCCTT  - CCCTTACCCGCATCTCCCAGGACGCCCCTT
SEQ ID NO:6 SEQ ID NO:7 SEQ ID NO:9 SEQ ID NO:10 SEQ ID NO:11 SEQ ID NO:11 SEQ ID NO:11	SEQ ID NO:14 SEQ ID NO:15 2. 'B' Allele	999999	SEQ ID NO:22 SEQ ID NO:23 SEQ ID NO:24 SEQ ID NO:25 SEQ ID NO:26

FIGURE 6A

## FIGURE 6B

3. 'C' Allele, CYP2D6\*9, G2702-A2704 deletion, decreased enzyme activity

# Appln. No. 09/880,732 Amendment dated October 25, 2004 Response to Drawing Requirement of August 25, 2004 Replacement Sheet

												Re	ep]	lac	en	ner	it S	She	eet								
	CYPwt(+)C2691, 22mer,55%GC, Tm=60C	CYPwt(+)C2691 (A)30-3'NH2	CYPwt(+)C2692 (A)30-3'NH2	CYPmut(+)C2691, 21mer, 57%GC, Tm=60C	CYPmut (+) C2691 (A) 30-3'NH2	CYPmut (+) C2692 (A) 30-3'NH2	(-) פראלי הרוֹשׁ	Mut (-)	zyme activity	E3009 (C/A to wt at base 15)		CYPwt(-)E3009, 19mer,53%GC, Pred Tm=57	CYPwt(-) E3009(A)30-3'NH2	CYPmut (+) E3009, 19mer, 58%GC, Pred Tm=59C	CYPmut(+) E3009(A)30-3'NH2		Wild Type(+)	Mut (+)		:/T to wt at base 6)	CYPwt(-)E3018,19mer,58%GC,Tm=60	CYPwt(+)E3018- Target	CYPmut (+) E3018, 19mer, 63%GC, Tm=62C	CYPmut(-) E3018- Target	 Wild Type(+)	Mut (+)	
-2702	5'- GCAGAGATGGAGAAGGTGAGAG -3'NH2	5'- GCAGAGATGGAGAAGGTGAGAG(A)30 -3' NH2	5'- CAGAGATGGAGAAGGTGAGAG(A)30 -3' NH2	5'- GCAGAGATGGAGGTGAGAGTG -3' NH2	5'- GCAGAGATGGAGGTGAGAGTG(A)30 -3' NH2	5'- CAGAGATGGAGGTGAGAGTG(A)30 -3' NH2	-2676 3'- TGACTFCGGAAGGAACGTCTCTCTAACCTCTTTTCCACTCTAACGAAGGAAG	TGACTCCGGAAGGACCGTCTCTACCT CCACTCTCACCGACGGTGCCAC	Allele, CYP2D6*7, A3023C, H324P amino acid change results in zero enzyme activity	A. wt Probe - CYPwt(-)E3009 (T/C to mut at base 5) & CYPmut(+)E3009 (C/A to wt	į	NH2 3'- CGAGTACTAGGATGTAGGC -5'	NH2 3'- (A) 30CGAGTACTAGGATGTAGGC -5'	5'- GCTCATGATCCTACCTCCG -3'NH2	5' - GCTCATGATCCTACCTCCG(A)30 -3'NH2	-2998		5'- TGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC GTGAGCCCATC -3'	-3038-Intron Start	B. $CYPwt(-)E3018$ (T/C to mut at base 14) and $CYPmut(+)E3018$ (C/T to wt at base 6)	GGATGTAGGCCTACACGTC	5'- CCTACATCCGGATGTGCAG -3'	5'- CCTACCTCCGGATGTGCAG -3' NH2	3'- GGATGGAGGCCTACACGTC -5'	TGGGGCCTCCTGCTCATGATCCTACATCCGGATGTGCAGC GTGAGCCCATC	5' - IGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC GTGAGCCCATC -3'	-3038-Intron Start
	ID NO:28	ID NO:29	ID NO:30	ID NO:31	ID NO:32	ID NO:33	TO MO.34	NO:35	'E' Allele,	æ		ID NO:36	ID NO:37	ID NO:38	ID NO:39		ID NO:40	ID NO:41		ш	ID NO:42	ID NO:43	ID NO:44	ID NO:45	NO:46	ID NO:47	
	SEQ	SEQ	SEQ	SEQ	SEQ	SEQ	OHO CHO		4.			SEQ	SEQ	SEQ	SEQ		SEQ	SEQ			SEQ	SEQ	SEQ	SEQ		SEQ	

### the and

CYPwt (+)G1840(A)30-3'NH2,18mer,67%GC, Tm=60

-3' NH2

5' - CACTCCGGTGGGTGATGG (A) 30

(A) 30GTGAGGCCACCACTACC

NH2 3'-

SEQ ID NO:49 ID NO:50 5, -

NO:51

SEQ ID

SEQ

NO:52

CYPmut (+) G1840 (A) 30-3'NH2, 18mer, 61%GC,

CYP2D6\*6, T1795 deletion, Frameshift resulting in zero enzyme activity

Allele,

GTGCCGCCTTCGCCACTCC GGTGGGTGATGGGCAGAAGGGCACAAAGCGGG -3' 5'- GTGCCGCCTTCGCCACTCC TGTGGGTGATGGGCAGAAGGGCACAAAGCGGG -3'

Exon 3 end- |-1846

5' - CACTCCTGTGGGTGATGG(A)30 -3' NH2

CYP2D6\*8, G1846T, Stop codon, zero enzyme activity

Allele,

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5.

FIGURE 6C

CYPwt(-) G1840(A)30-3'NH2

SEQ ID NO:53	5'- GCTGGAGCAGTGGGTGAC -3' NH2	CYPwt(+) T1785, 18mer, 67%GC, Trn=59-61C
SEQ ID NO:54	5' - GCTGGAGCAGTGGGTGAC(A)30 -3' NH2	CYPwt (+) T1785 (A) 30-3'NH2
SEQ ID NO:55	5' - CTGGAGCAGTGGGTGAC(A)30 -3' NH2	CYPwt(+)T1786 (A)30-3'NH2
SEQ ID NO:56	5'- GCTGGAGCAG-GGGTGAC -3' NH2	CYPmut(+)T1785, 17mer,71 %GC, Tm=58-60C
SEQ ID NO:57	5'- GCTGGAGCAG-GGGTGAC(A)30 -3' NH2	CYPmut (+) T1785 (A) 30-3'NH2
SEQ ID NO:58	5'- CTGGAGCAG-GGGTGAC(A)30 -3' NH2	CYPmut (+) T1786 (A) 30-3'NH2
	-1773	
SEQ ID NO:59	5'-GGGCAAGAAGTCGCTGGAGCAGTGACCGAGGAGGCCGCCTGCCT	3' Wild Type(+)
SEQ ID NO:60	5'-GGGCAAGAAGTCGCTGGAGCAG-GGGTGACCGAGGAGGCCGCCTGCCT -3'	3' Mut(+)
7. 206/207/20	7. 2D6/2D7/2D8 Controls - The 2D6/7/8 probes were designed in the 1600 region of the 2D6 gene. The purpose of th	500 region of the 2D6 gene. The purpose of th
designs was t	designs was to find region somewhere between the PCR primers were	ere between the PCR primers were it would be easy to discriminate between 2D6 a
its two pseud	its two pseudogenes, 2D7 and 2D8. The purpose of the designs is to	The purpose of the designs is to demonstrate that the PCR amplicon is from the
2D6 gene, not	gene, not one of the pseudogenes.	
SEQ ID NO:61	5'- GACCAGGGGAGC-ATAGG(A)30-3' NH2	CYP2D6wt (+) 1607 (A) 30-3'NH2
SEQ ID NO:62	5'- GACCTTGTGGAGCGCCAG(A)30-3' NH2	CYP2D7wt (+) 1607 (A) 30-3'NH2
SEQ ID NO:63	5'- GACCAGGAAAAGC-ACAGG(A)30-3' NH2	CYP2D8wt (+) 1607 (A) 30-3'NH2
SEQ ID NO:64	5'- GACCAGGAAAGC-ACAGGG(A)30-3' NH2	CYP2D8wt(+) 1607b (A) 30-3'NH2
	-1603	
SEQ ID NO:65	5' - GGGAGACCAGGGGGAGC-ATAGGGTTGGAGTGGGTGGT -3'	2D6 (+)
SEQ ID NO:66	5' - GGGAGACCTTGTGGAGCGCCAGGGTTGGAGTGGGTGGC -3'	2D7 (+)

8. Pos/Neg Control probes- These probes were designed as true positive and negative control probes. They consist

2D8 (+)

the same semi-random sequence, with the positive control probe having a

GGGAGACCAGGAAAAGC-ACAGGGTTGGAGTGGGCGGC

2, 2,

NO:67

SEQ

CYP(+)ran(A)25-5'Biotin,3'NH2 CYP(+)ran(A)25-3'NH2

NH2 NH2

5' Biotin- ATCATTCCAATCATCCATATCATC(A)25 -3'
5'- ATCATTCCAATCATCCATATCATC(A)25 -3'

SEQ ID NO:68 SEQ ID NO:69

5' Biotin.